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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,007	11/20/2003	Randolph Mellus Johnson	DURE-007CON2	9101

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EXAMINER
GHALI, ISIS A D

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
08/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/719,007	**Applicant(s)** JOHNSON ET AL.	
	Examiner Isis A. Ghali	**Art Unit** 1611	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 August 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on *08/02/2010*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Isis A Ghali/
Primary Examiner, Art Unit 1611

Continuation of 11. does NOT place the application in condition for allowance because:

Claims 48-56, 58-67, 69-72, 74-81,83-91 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the article "Analgesia and sedation with sufentanil in intensive care medicine" by Wappler et al. combined with article "Long term spinal therapy in terminally ill cancer patients" by Wagemans et al., Peterson et al. (US 6,524,305) and Nelson et al. (US 5,980,927).

Applicants argue that the combination of references fails to teach or suggest each and every element of the claims. Wappler teaches IV administration and fails to teach or suggest a sufentanil in the claimed concentration and Wagemans teaches epidural and intrathecal administration. Wagemans indirects one of ordinary skill in the art away from a method as presently claimed which requires systemically administering sufentanil.
In response to this argument, it is argued that Wappler clearly teaches that the administration of sufentanil is suitable for intensive care patients for systemic sedation and analgesia without significant respiratory depression during spontaneous breathing. Therefore systemic administration is taught by Wappler. Further the daily dose in mg/ml of 250.25 mg delivered at the lowest delivery rate of 0.01 ul/day will provide low delivery rate as low as 0.0025 mg/day to 1000 mg/day if delivery rate is 2 ml/day, i.e. 2.5-1000,000 ug/day. Present claim 84 recites 0.01 ug/hour to about 200 ug/hour. In other words, Wappler teaches delivery of the same amount of sufentanil per day, and teaches the same delivery rate, and this suggests the same total concentration in device as instantly claimed. Therefore, the claimed delivery rates of sufentanil are taught by the Wappler, and the claimed delivery rates disclosed by the reference fall within the broad claimed delivery rates. Wappler teaches low dosage and dose is expected to be less for debilitating or patients with lighter weights. Wappler further suggested that dose can be adjusted according to patient requirement, i.e. can be reduced to the claimed ranges. Both references disclose un-interrupted delivery of the analgesics once the desired level to induce analgesia is achieved. The claims do not require any specific site of administration, therefore, epidural and administration is encompassed by the claims. Wagemans teaches long-term opioid profound therapy, i.e. not only at the site of administration, with minimal side effects and efficacy throughout the body and for different types of pain, and further teaches sufentanil is a preferred analgesic in minimal effective dose. Wagemans teaches systemic absorption of opioids delivered by epidural and intrathecal routes. Wagemans discussed both local and systemic administration of opioids. Wagemans teaches local delivery that provides both systemic and local analgesic effects by teaching "efficacy throughout the body and for different types of pain are important advantages." Although Wagemans teaches advantages of local administration, the reference further teaches in page 72, right column that "Both epidural and intrathecal routes have advantages and disadvantages". Therefore, every route of administration, either local or systemic has its own advantage and disadvantage. It is further argued that, even with local administration, it is inevitable to have some opioid absorbed systemically from the local administration site to provide systemic effect. Additionally, Wagemans teaches delivery by implanted infusion pump for months or years and provides constant infusion. Therefore, constant infusion for long periods of minimal effective dose of sufentanil for systemic effect is taught by Wagemans. Wappler disclosed continuous pump infusion. Both Wagemans and Wappler teach method of delivery of sufentanil by infusion and both teach systemic delivery, however, Wappler preferred intravenous infusion and Wagemans preferred spinal infusion. The present claims are not directed to any specific site of delivery of sufentanil. The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Applicants argue that no apparent reason to combine Wappler with Wagemans in combination with Peterson and Nelson. Nelson teaches away from the proposed combination of references which includes Wappler because Nelson provides a device and method for administering an analgesic directly to the neuraxis of an organism, therefore teaches away from the systemic administration.
In response to this argument, it is argued that Peterson teaches the low delivery volume rate for long time. The implantable devices that deliver low volume for extended periods were known at the time of the invention and taught by Peterson. Further Peterson suggested delivery of analgesics, and Wagemans desired long term opioid therapy. Therefore, at the time of the invention, one having ordinary skill in the art would have used the implantable osmotic device disclosed by Peterson to deliver sufentanil in the doses disclosed by the combination of Wappler and Wagemans. Nelson teaches prolonged delivery of analgesics by implanted devices over periods extends up to one year. Table I of the reference teaches that loading dose sufficient for long period administration, e.g. six month dose, can be calculated if the daily dose is known and this would suggest o one having ordinary skill in the art that it is possible to calculate the required does of sufentanil to be loaded in implantable device for long term therapy. Nelson exemplified fentanyl, however, teaches prolonged delivery of analgesics and recommended sufentanil because of its potency. Nelson teaches treatment of chronic pain, and does not limit the site of pain. Therefore, any kind of pain at any part of the body will be treated by the implantable device of Nelson. Wappler disclosed continuous delivery by i.v. Both Nelson and Wappler teach method of continuous prolonged delivery of sufentanil and both teach systemic delivery. It is further argued that, even with local administration, it is inevitable to have some opioid absorbed systemically from the local administration site to provide systemic effect, Nelson is relied upon for teaching that it is possible to calculate the dose to be loaded in an implantable device if the daily dose and period of administration are known. The present claims are not directed to any specific site for delivery of sufentanil. The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Therefore, Nelson does not teach away from Wappler, nor deter one having ordinary skill in the art to combine Nelson with Wappler and Wagemans. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." In re Gurley, 27 F.3d 551,553 (Fed. Cir. 1994).